

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte THOMAS KIY, and
RUDIGER MARQUART

Appeal No. 2001-0380
Application No. 08/676,971

ON BRIEF

Before ADAMS, MILLS and GREEN, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-14, which are all the claims pending in the application.

Claim 1 is illustrative of the subject matter on appeal and is reproduced below:

1. A method for culturing ciliates, comprising the steps of:
placing ciliates and medium therefor in a culture flask;
providing said culture flask with a stirrer having a magnetic core,
wherein said stirrer is suspended in the top part of the culture flask
such that the stirrer does not touch the flask bottom, and wherein the
motion of said stirrer is driven by means of a magnetic field; and
stirring said ciliates in said culture medium.

The references relied upon by the examiner are:

Wergeland et al. (Wergeland) 5,008,197 Apr. 16, 1991

Hofmann et al. (Hofmann), "External Factors Limiting the Multiplication Potential of Tetrahymena," J. Cell Sci., Vol. 50, p. 407-418 (1981)

Griffiths, "Scaling-up of Animal Cell Cultures" Animal Cell Culture: a practical approach, Chp. 3, pp. 33-39 (1987)

Lognay et al. (Lognay), "Improvement of Fed Batch Mass Culture for γ Linolenic Biosynthesis by Tetrahymena Rostrata," Biotechnology Letters, Vol. 11, No. 6, pp. 423-426 (1989)

GROUND OF REJECTION

Claims 1, 2 and 5-9 stand rejected under 35 U.S.C. § 103 as obvious over Hofmann in view of Wergeland and Griffiths.

Claims 1, 3, 4 and 10-14 stand rejected under 35 U.S.C. § 103 as obvious over Hofmann in view of Wergeland, Gosselin and Griffiths.

We reverse.

DISCUSSION

Claims 1, 2 and 5-9:

According to the examiner (Answer, page 4), Hofmann "teach a method for culturing the ciliates, Tetrahymena, which belong to the group Holotrichia, comprising the steps of placing ciliates in an Erlenmeyer flask containing media and shaking the flask at a low speed to avoid generation of foam...." The examiner recognizes, however, that Hofmann "do not teach stirring the ciliates with a magnetic stirrer at a particular speed, nor ... a membrane aeration stirrer or stirring by a reciprocating mixing technique." Id. To make up for these deficiencies in Hofmann, the examiner relies on Wergeland and Griffiths.

The examiner relies on Wergeland (id.) to "teach a method and device for improving oxygenation of fragile cells in culture ... wherein mammalian cells in

medium are stirred with a suspended aeration membrane stirrer driven by a magnetic field....” With regard to Griffiths, the examiner finds (id.) Griffiths “teaches that magnetic drive stirrers provide a more homogeneous liquid/cell suspension via axial and radial flow as well as laminar and turbulent mixing....”

In response, appellants argue (Brief, page 7), the art relied up by the examiner discusses mammalian cells, and does not suggest the use of “stirrer technology for culturing ciliates ... [which] are sensitive to shear forces and were not though to be amenable to techniques that involve a high degree of physical disruption.” Appellants refer to the Kiy Declaration to support this position. According to Kiy (Declaration, paragraph 4), “[c]iliates belong to the most sensitive of all cells to shear forces and that mammalian cells, on the other hand, are either adapted to with stand shear force or are treated in such a way as to lessen the negative effect of shear force.” Therefore appellants argue (Brief, page 7), “the skilled artisan would not reasonably expect to use stirring with ciliates, since such a technique would be expected to break these fragile cells.”

Upon review of the references, we note that Wergeland disclose (Column 1, lines 12-16), “the invention is concerned with the oxygenation of biological cultures using so-called microcarrier techniques, wherein e.g., tissue cells or mammalian cells are grown on a solid surface in the form of small carrier beads.”¹ Example 7 of Wergeland as relied upon by the examiner (Answer, page 4, “column 7, lines 31-36”), requires the use of “cells cultivated on microcarriers (see column 7, line 6). We also note that as relied upon by the

¹ We note that there is no evidence on this record that ciliates are grown on microcarriers.

examiner (Answer, page 4) Griffiths (page 55, Figure 8, examples D-F), discuss the “[t]ypes of impellers for growing suspension and microcarrier cells.” As the examiner explains (Answer, page 4), “magnetic drive stirrers provide a more homogeneous liquid/cell suspension via axial and radial flow as well as laminar and turbulent mixing.” However, Griffiths teaches (page 62), “[t]he energy generated at the tip of the stirrer blade is a limiting factor as it gives rise to a damaging shear force. Shear forces are created by fluctuating liquid velocities in turbulent areas.” According to Griffiths (page 63), “[t]he greater the turbulence the more efficient the mixing, but a compromise has to be reached so that cells are not damaged.” As Griffiths point out (id.), “[i]f the cells are too fragile for stirring, or if sufficient mixing cannot be obtained without causing unacceptable shear rates then an alternative mixing system may have to be used.”

In response, the examiner maintains (Answer, page 14):

one of ordinary skill in the art would have had a high expectation of successfully maintaining high growth levels and minimizing cell damage, i.e., foaming, of the fragile ciliates by modifying the culture method of Hofmann et al. to gently mix the cells and medium with overhead magnetic stirring, and to renew nutrients by batch-fed or cyclic medium exchange methods.

The examiner, however, identifies no evidence to support this conclusion. In this regard, we remind the examiner that “[t]he consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art.” In re Dow Chemical Co. 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

Furthermore, as set forth in In re Kotzab, 217 F.3d 1365, 1369-70, 55

USPQ2d 1313, 1316 (Fed. Cir. 2000):

A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. ... Close adherence to this methodology is especially important in cases where the very ease with which the invention can be understood may prompt one “to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher.”

...

Most if not all inventions arise from a combination of old elements. ... Thus, every element of a claimed invention may often be found in the prior art. ... However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. ... Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. [Citations omitted].

On this record, we agree with appellants that the examiner failed to identify where the prior art of record provides the requisite suggestion to make the specific combination leading to appellants’ claimed invention. In our opinion, the statement of the rejection, at best, establishes that individual parts of the claimed invention were known in the prior art. The statement of the rejection, however, fails to establish that a person of ordinary skill in the art would have a reasonable expectation of success in combining the elements disclosed in the prior art in the manner necessary to arrive at appellants’ claimed invention. Therefore, it is our

opinion that the examiner failed to meet her burden² of establishing a prima facie case of obviousness.

Accordingly we reverse the rejection of claims 1, 2 and 5-9 under 35 U.S.C. § 103 as obvious over Hofmann in view of Wergeland and Griffiths.

Claims 1, 3, 4 and 10-14:

The examiner relies on Hofmann, Wergeland and Griffiths as above in addition to noting that Griffiths also teaches (Answer, page 6) “a cyclic medium exchange method of culturing cells comprising the intermittent replacement of a constant fraction of the culture with an equal volume of medium.” In addition, the examiner finds that Gosselin (id.), “teach a method of culturing Tetrahymena by a batch-fed culture system which results in a doubling of cell growth compared to a simple batch culturing technique....”

Gosselin’s batch culture techniques, however, fail to make up for the deficiencies, see supra, in the combination of Hofmann, Wergeland and Griffiths.

² The initial burden of presenting a prima facie case of obviousness rests on the examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

Accordingly, we reverse the rejection of claims 1, 3, 4 and 10-14 under 35 U.S.C.
§ 103 as obvious over Hofmann in view of Wergeland, Gosselin and Griffiths.

REVERSED

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